

REMARKS

I. Status of the Claims

Claims 1-10 have been canceled, and claims 11-24 have been added. Thus, claims 11-24 are pending, have been examined, and stand rejected under 35 U.S.C. §112, first paragraph and 35 U.S.C. §112, second paragraph. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Clarification

In the Communication mailed on May 22, 2002, it is indicated that applicants had failed to respond to the "written description" rejection of claims 11-24 on the grounds that a FKHL7 bioactivity is not provided, citing the Office Action at page 5. However, the FKHL7 bioactivity rejection given at that page is an *enablement* rejection. Thus, applicants will address it as such in §IV below.

III. Formalities

The examiner has requested a sequence listing in accordance with 37 C.F.R. §1.821. A sequence listing was filed with applicants' previous submission, as was an amendment to the Brief Description of the Drawings. Also, amendment of page 92 of the specification was provided.

IV. Rejections Under 35 U.S.C. §112, First Paragraph

Claims 11-24 stand rejected as allegedly lacking both written description of the claimed invention, and an enabling disclosure. Applicants respectfully traverse.

First, the examiner argues that the claims are overly broad in referring to FKHL7 proteins and genes generally, and presumably that they should be limited to the exemplified sequences. Applicants traverse the rejection but, in the interest of advancing the prosecution, they have amended the claims to include reference to the sequence of SEQ ID NO:2. Thus, the rejection is believed to be overcome.

Next, it is argued that applicants have failed to identify any binding partners of FKHL7. Applicants submit that FKHL7 contains a consensus binding site of RTAAAYA found in four other FKHL-7 proteins. This molecule is thus properly characterized as a DNA binding protein, and in the context of this assay, applicants submit that DNA could be utilized as a binding partner. Thus, one of skill in the art would both apprehend and be able to practice this aspect of the invention without undue experimentation. Thus, it is respectfully submitted that the instant claims are indeed adequately described and enabled.

The examiner also objects to the claims 14 and 24 as the specification allegedly describes no such compounds, much less fails to disclose any particular structures for such compounds. Applicants traverse. Claims 14 and 24 are "product-by-process" claims. Such claims are specifically contemplated where it is difficult or impossible to define products by their physical characteristics, *i.e.*, their structure. *In re Steppan et al.*, 156 USPQ 143 (CCPA 1967); *Ex parte Brian et al.*, 118 USPQ 242 (BPAI 1958). Product claims may include process steps that either partially or wholly define the claimed product. *In re Hallman*, 210 USPQ 609 (CCPA 1981).

Thus, the stated ground for rejection – that the claims are product-by-process – is insufficient to make out a *prima facie* case for lack of written description.

Finally, the examiner believes that the specification fails to provide any bioactivity for FKHL7. Thus, it is argued that one could not practice the present claims as the bioactivity to be assayed for is not stated. As the examiner points out, the specification provides not one but *two* bioactivities for FKHL7 – DNA binding and induction of transcription. Those of skill in the art, with only this disclosure, would immediately recognize a multitude of assays in which these bioactivities could be assessed. For example, DNA binding can be assessed by passing radiolabeled genomic sequences over an FKHL7 column – retention of radioactive “counts” reveals DNA binding. Similarly, induction of gene expression can be assessed simply by measuring increased transcription in either whole cell or cell-free systems. A particular gene target is not required – rather, total incorporated radioactivity (using labeled nucleotides) or 2-dimensional gel analysis can be employed. Applicants emphasize that it is the examiner’s burden to come forward with evidence or scientific reasoning as to why applicants’ presumptively enabling disclosure is, in fact, non-enabling. Clearly, the rejection here fails to meet this burden.

In light of the preceding, applicants respectfully request reconsideration and withdrawal of the rejection.

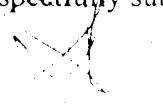
V. Rejections Under 35 U.S.C. §112, Second Paragraph

The examiner has rejected each of claims 11 and 15-21 as allegedly indefinite. Applicants have provided amendments that are believed to address each of the rejections. Reconsideration and withdrawal of the rejections is therefore respectfully requested.

VI. Summary

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned at (512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application. Please date stamp and return the enclosed postcard as evidence of receipt.

Respectfully submitted,


Steven L. Highlander
Reg. No. 37,642
Attorney for Applicant

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 536-3184

Date: June 24, 2002

RECEIVED



APPENDIX A1: MARKED UP COPY OF CLAIMS

JUL 08 2002

TECH CENTER 1600/2900

11. (Amended) A method for identifying a compound that modulates an FKHL7 bioactivity, comprising the steps of:

- (a) contacting [an appropriate amount of] the compound with a cell or cellular extract, which expresses an FKHL7 gene having the amino acid sequence of SEQ ID NO:2; and
- (b) determining the resulting FKHL7 bioactivity,

wherein an increase or decrease in the FKHL7 bioactivity in the presence of the compound as compared to the bioactivity in the absence of the compound indicates that the compound is a modulator of an FKHL7 bioactivity.

15. (Amended) The method of claim 11, wherein the compound is [a member] selected from the group consisting of a polypeptide, a nucleic acid, a peptidomimetic, and a small molecule.

16. (Amended) The method of claim [11] 15, wherein the small molecule is a steroid.

17. (Amended) The method of claim [11] 15, wherein the nucleic acid is a member selected from the group consisting of a gene replacement, an antisense, a ribozyme, and a triplex nucleic acid.

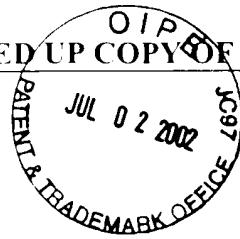
18. (Amended) A method for identifying a compound that modulates an FKHL7 bioactivity comprising the steps of:

- (a) combining an FKHL7 protein having the amino acid sequence of SEQ ID NO:2, and FKHL7 binding partner, and a test compound under conditions wherein, but for the test compound, the FKHL7 protein and FKHL7 binding partner are able to interact; and
- (b) detecting the formation of an FKHL7 protein FKHL7 binding partner complex.

such that a difference in the formation of an FKHL7 protein/FKHL7 binding partner complex in the presence of a test compound relative to in the absence of the test compound indicates that the test compound is a modulator of an FKHL7 [therapeutic].

19. (Amended) The method of claim 18, wherein the compound is [a member] selected from the group comprising a polypeptide, a nucleic acid, a peptidomimetic, and a small molecule.
20. (Amended) The method of claim [18] 19, wherein the small molecule is a steroid.
21. (Amended) The method of claim [18] 19, wherein the nucleic acid is a member selected from the group consisting of a gene replacement, an antisense, a ribozyme, and a triplex nucleic acid.

APPENDIX A2: MARKED UP COPY OF SPECIFICATION



Fourth full paragraph at page 7:

[**Figure 1** is] FIGS. 1A-1B are a DNA sequence of the human FKHL7 gene including the 5' and 3' untranslated regions (UTRs) (SEQ ID No. 1). The 1659 base pair open reading frame is provided herein as SEQ ID NO. 3 and the (SEQ ID NO. 3) 553 amino acid human FKHL7 protein is provided herein as SEQ ID No. 2. The forkhead region of the protein is indicated by underline.

Paragraph bridging pages 7-8:

[**Figure 2**] FIG. 2 shows an amino acid comparison of the forkhead domains of different members of the FKHL-family of genes. The locations of the three alpha helices and the two wing domains are shown (Clark, K.L. et al., Nature 364:412:420 (1993)). The *Drosophila* forkhead gene sequence is shown above that for *FKHL7*, while the positions of the three missense mutations are shown below *FKHL7*. Translation of the 11 base pair deletion (bp del) mutation results in total loss of the forkhead domain. The other FKHL family members are shown below *FKHL7* for comparison. For *FKHL10*, only partial sequence is available for forkhead domain. The last sequence shown is that for the distantly related *FKHR* which has been mapped to 13Q14 near the *RIEG2* locus.

First full paragraph age page 8:

[**Figure 3**] FIG. 3 provides the identity and location of Expressed Sequence Tags (ESTs) that map to regions of the human FKHL7 gene.

Paragraph bridging pages 91-92:

An 11 bp deletion upstream of the *FKHL7* forkhead domain was identified in two brothers diagnosed with different anterior segment defects (RA and IH). Both brothers had

glaucoma, and neither had the extra-ocular manifestations of Reiger syndrome (RS). Their father was found to have isolated posterior embryotoxon (PE), suggesting that the disease was inherited through him as an autosomal dominant. He was also found to carry the deletion. A second mutation was found in a proband and her mother who were both diagnosed with classic RA and glaucoma. This mutation, a C to T transition within the forkhead domain causes a change from a serine to a leucine (SER131Leu). A third mutation, a C to G transversion within the forkhead domain, was found in a proband with severe Axenfeld anomaly and glaucoma. This change results in the replacement of isoleucine with methionine (Ile126MET) and is also found in the father who was diagnosed with AA. Finally, a T to C transition was found in a proband of an extended family with a spectrum of anterior segment defects. This change results in the replacement of phenylalanine with serine (Phe112Ser) within the forkhead domain. [The pedigrees of each family (Fig. 6) and the associated mutations (Fig. 7) are shown.] Three of the mutations were not found in 128 unrelated normal individuals from an ethnically similar control population (Caucasian). The fourth mutation (Phe112Ser) was only detected by direct sequencing of PCR products from patient genomic DNA. This mutation was found to segregate with the disease in an extended pedigree and was not present in an additional 12 Caucasian individuals by sequence analysis.

RECEIVED
JUL 02 2002
U.S. PATENT & TRADEMARK OFFICE
CUSTOmer SERVICE CENTER

RECEIVED

JUL 08 2002

TECH CENTER 1600/2900

APPENDIX B1: CLEAN COPY OF PENDING CLAIMS

11. A method for identifying a compound that modulates an FKHL7 bioactivity, comprising the steps of:
 - (a) contacting the compound with a cell or cellular extract, which expresses an FKHL7 gene having the amino acid sequence of SEQ ID NO:2; and
 - (b) determining the resulting FKHL7 bioactivity,
wherein an increase or decrease in the FKHL7 bioactivity in the presence of the compound as compared to the bioactivity in the absence of the compound indicates that the compound is a modulator of an FKHL7 bioactivity.
12. The method of claim 11, wherein the compound is an agonist of an FKHL7 bioactivity.
13. The method of claim 11, wherein the compound is an antagonist of an FKHL7 bioactivity.
14. A compound that has been identified according to the method of claim 11.
15. The method of claim 11, wherein the compound is selected from the group consisting of a polypeptide, a nucleic acid, a peptidomimetic, and a small molecule.
16. The method of claim 15, wherein the small molecule is a steroid.
17. The method of claim 15, wherein the nucleic acid is a member selected from the group consisting of a gene replacement, an antisense, a ribozyme, and a triplex nucleic acid.
18. A method for identifying a compound that modulates an FKHL7 bioactivity comprising the steps of:
 - (a) combining an FKHL7 protein having the amino acid sequence of SEQ ID NO:2, and FKHL7 binding partner, and a test compound under conditions wherein, but

for the test compound, the FKHL7 protein and FKHL7 binding partner are able to interact; and

(b) detecting the formation of an FKHL7 protein/FKH7 binding partner complex, such that a difference in the formation of an FKHL7 protein/FKHL7 binding partner complex in the presence of a test compound relative to in the absence of the test compound indicates that the test compound is a modulator of an FKHL7.

19. The method of claim 18, wherein the compound is selected from the group comprising a polypeptide, a nucleic acid, a peptidomimetic, and a small molecule.
20. The method of claim 19, wherein the small molecule is a steroid.
21. The method of claim 19, wherein the nucleic acid is a member selected from the group consisting of a gene replacement, an antisense, a ribozyme, and a triplex nucleic acid.
22. The method of claim 18, wherein the compound is an agonist of on FKHL7 bioactivity.
23. The method of claim 18, wherein the compound is an antagonist of on FKHL7 bioactivity.
24. A compound that has been identified according to the method of claim 18.

RECEIVED

APPENDIX B2: CLEAN COPY OF SPECIFICATION

JUL 08 2002

TECH CENTER 1600/2900

Fourth full paragraph at page 7:



FIGS. 1A-1B are a DNA sequence of the human FKHL7 gene including the 5' and 3' untranslated regions (UTRs) (SEQ ID No. 1). The 1659 base pair open reading frame is provided herein as SEQ ID NO. 3 and the (SEQ ID NO. 3) 553 amino acid human FKHL7 protein is provided herein as SEQ ID No. 2. The forkhead region of the protein is indicated by underline.

Paragraph bridging pages 7-8:

FIG. 2 shows an amino acid comparison of the forkhead domains of different members of the FKHL-family of genes. The locations of the three alpha helices and the two wing domains are shown (Clark, K.L. et al., Nature 364:412:420 (1993)). The *Drosophila* forkhead gene sequence is shown above that for *FKHL7*, while the positions of the three missense mutations are shown below *FKHL7*. Translation of the 11 base pair deletion (bp del) mutation results in total loss of the forkhead domain. The other FKHL family members are shown below *FKHL7* for comparison. For *FKHL10*, only partial sequence is available for forkhead domain. The last sequence shown is that for the distantly related *FKHR* which has been mapped to 13Q14 near the *RIEG2* locus.

First full paragraph age page 8:

FIG. 3 provides the identity and location of Expressed Sequence Tags (ESTs) that map to regions of the human FKHL7 gene.

Paragraph bridging pages 91-92:

An 11 bp deletion upstream of the *FKHL7* forkhead domain was identified in two brothers diagnosed with different anterior segment defects (RA and IH). Both brothers had

glaucoma, and neither had the extra-ocular manifestations of Reiger syndrome (RS). Their father was found to have isolated posterior embryotoxon (PE), suggesting that the disease was inherited through him as an autosomal dominant. He was also found to carry the deletion. A second mutation was found in a proband and her mother who were both diagnosed with classic RA and glaucoma. This mutation, a C to T transition within the forkhead domain causes a change from a serine to a leucine (SER131Leu). A third mutation, a C to G transversion within the forkhead domain, was found in a proband with severe Axenfeld anomaly and glaucoma. This change results in the replacement of isoleucine with methionine (Ile126MET) and is also found in the father who was diagnosed with AA. Finally, a T to C transition was found in a proband of an extended family with a spectrum of anterior segment defects. This change results in the replacement of phenylalanine with serine (Phe112Ser) within the forkhead domain. Three of the mutations were not found in 128 unrelated normal individuals from an ethnically similar control population (Caucasian). The fourth mutation (Phe112Ser) was only detected by direct sequencing of PCR products from patient genomic DNA. This mutation was found to segregate with the disease in an extended pedigree and was not present in an additional 12 Caucasian individuals by sequence analysis.